

In the Specification

On page 4, amend the paragraph at lines 10-11 to add a period at the end of the sentence as follows:

Fig. 1 Scheme of the method for detection of thrombolytic action of drugs *in vivo* in rats (according to Gryglewski).

On page 4, amend the paragraph at lines 12-13 to add a period at the end of the sentence as follows:

Fig. 2 Thrombolytic response induced by intravenous administration of MNA+
in vivo (30 mg/kg).

On page 4, amend the paragraph at lines 14-15 to add a period at the end of the sentence as follows:

Fig. 3 Changes in plasma levels of 6-keto-PGF_{1α} (●) and TXB₂ (○) after intravenous administration of MNA+ (30 mg/kg).

On page 4, amend the paragraph at lines 20-21 to add a period at the end of the sentence as follows:

Fig. 6 Thrombolytic response induced by intravenous administration of MAP⁺ in vivo (30 mg/kg).

On page 4, amend the paragraph at lines 22-23 to add a period at the end of the sentence as follows:

Fig 7 Changes in plasma levels of 6-keto-PGF_{1α} (●) and TXB₂ (○) after intravenous administration of MAP⁺ in vivo (30 mg/kg).

On page 4, amend the paragraph at lines 24-25 to add a period at the end of the sentence as follows:

Fig. 8 Thrombolytic response induced by intravenous administration of MNAF⁺ (30 mg/kg).

On page 4, amend the paragraph at lines 26-27 to add a period at the end of the sentence as follows:

Fig. 9 Lack of effect of MNA⁺ on collagen-induced aggregation of platelets (1 mg/ml).

On page 4, amend the paragraph that begins on line 28 to add a period at the end of the sentence as follows:

Fig. 10 Lack of effect of MNA⁺ on latex-induced activation of neutrophils.

At page 7, amend the last paragraph as below:

The invention in the second aspect provides a method of treatment and/or prevention of conditions or diseases associated with dysfunction of vascular endothelium, oxidative stress, and/or insufficient production of endothelial PGI₂ (associated or not with hypercholesterolemia, hypertriglyceridemia or a low HDL level), in particular such as discussed above, comprising administration to a subject in [[a]] need of such treatment a therapeutically effective amount of a quaternary pyridinium salt of formula I as defined above.

On page 12, amend the third full paragraph as follows:

During the initial 20-30 min of superfusion the strip gained was gaining in weight by 80-120 mg in weight because of the deposition of platelet-rich thrombi [[_]] and then in control conditions stayed unchanged during the next 3-5 hrs. A thrombolytic Thrombolytic response was detected by a fall in weight weight of a thrombi. Arterial blood pressure was also monitored, so this model enabled the analysis of thrombolytic and hypotensive action of a compound (Fig. 1).

At page 12, amend the last full paragraph as follows:

The analysis of the thrombolytic response in this experimental set-up was complemented by the assay of 6-keto-PGF_{1α}, TXB₂ and PGE₂ in arterial blood plasma. For this purpose blood samples (500 µl) were collected in EPPENDORF® [[Eppendorff]] tubes with indomethacin to yield its final concentration of 10 µM, and EDTA to yield the final concentration of 1 mM. Then, the blood samples were spun spinned for 5 min at 2.000 x g. Plasma samples were stored at -70°C. The prostanoids were assayed using the enzyme immunoassay kits (Cayman Chemical Co, Ann Arbor, MI).

At page 12, amend the paragraph that being on line 30 as follows:

Intravenous administration of MNA (3-30 mg/kg) produced a concentration-dependent thrombolysis in Wistar rats with extracorporeal circulation. A maximum response was observed at the MNA⁺ dose of 30 mg/kg. Single injection of MNA⁺ at a dose of 30 mg/kg induced a long-lasting thrombolytic response at the level of 42± 4 % and remained at approximately the same level for 2-3 hours of the observation period. In contrast to MNA⁺, nicotinamide, nicotinic acid, trigonelline and 2-PYR (endogenous metabolite of MNA⁺), each of them at 30 mg/kg, failed to induce a significant thrombolytic response. Nicotinamide and nicotinic acid-induced responses were transient (less than 15-20 minutes) and at their maximum amounted merely to 9±0.6 %, 5±0.9 %, respectively). Trigonelline did not produce any thrombolytic response and response to 2-PYR was also very weak (<10 %) and transient (<15 min). The potency and duration of

thrombolytic responses to MNA⁺, nicotinamide and nicotinic acid correlated with a pattern of 6-keto-PGF_{1α} release to arterial plasma induced by these compounds. MNA⁺ (30 mg/kg) induced a substantial increase in levels of 6-keto-PGF_{1α} as early as 15 minutes after drug injection (from 104±7 to 460±58 pg/ml) which then [[than]] reached its plateau of around 400 pg/ml for at least one hour. On the other hand neither TXB₂ nor PGE₂ levels changed significantly in response to MNA⁺. The sluggish Sluggish rise in TXB₂ levels was time-dependent and observed also after saline injection. Levels of 6-keto-PGF_{1α} did not increase after injection of nicotinamide or after injection of nicotinic acid (30 mg/kg).

At page 14, line 10, amend the title of Example 2 as follows:

An anti-arthrogenic ~~ant-arthrogenic~~ effect in vivo in patients